

# THE SEARCH FOR A VACCINE FOR SYPHILIS\*

## AN EPIDEMIOLOGICAL APPROACH

BY

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Attempts to devise a vaccine against syphilis have been pursued for decades but thus far with little success. For the most part investigations have been focused on *Treponema pallidum*, modified in various ways, on the Reiter treponeme and its protein fractions, and on the closely related *Borrelia* organism.

Inoculation with *Treponema pallidum* produces a degree of immunity to re-infection and Neisser (1911) and others suggested that this immunity persisted as long as the original infection was maintained. Chesney (1926) postulated that resistance to re-infection was proportional to the duration of the original disease; even after treatment the immunity would still persist so long as the duration of the original infection, before treatment, had been sufficient. Magnuson, Thomas, Olansky, Kaplan,

de Mello, and Cutler (1956) confirmed these postulates by inoculating 62 syphilitic and non-syphilitic volunteers intracutaneously with varying amounts of *Treponema pallidum* (Nichols strain). His results demonstrated that the longer the patient had had syphilis before treatment the less was his chance of becoming re-infected; five of the volunteers were suffering from untreated latent syphilis and all five showed neither clinical nor serological response to the challenge.

The search for a syphilis vaccine leads naturally in the direction of developing or finding an attenuated treponeme which will cause a protective antibody response but no destructive lesions. If syphilis and the endemic treponematoses are listed in the order of their capacity to produce disease (Table I), syphilis—being pathogenic to all body systems and transmissible congenitally—clearly heads the list. Bejel follows, being responsible for

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TABLE I  
EPIDEMIOLOGY OF THE TREPONEMATOSSES

Character	Syphilis	Bejel (Endemic syphilis)	Yaws	Pinta
Organism	<i>T. pallidum</i> I	<i>T. pallidum</i> II	<i>T. pertenue</i>	<i>T. carateum</i>
Source	Genitalia, skin, mucous membranes	Buccal mucosa	Skin	Skin
Transmission	Venereal Congenital	Non-venereal Direct contact	Non-venereal Direct contact	Non-venereal Direct contact
Lesions: Initial site Skin Bone Heart, brain	Genital Moderate Moderate Moderate	Mouth Limited Moderate Scanty or absent	Skin, legs Extensive Scanty Absent	Exposed skin Extensive Absent Absent
Periods of latency	Characteristic	Characteristic	Characteristic	Absent
Age group of initial infection	Adults	Children	Children	Children
Distribution	Worldwide	Eastern Mediterranean North Africa	Tropical humid countries around Equator	Mexico Central America Venezuela

lesions of skin and bone, and possibly, on rare occasions, for cardiovascular and central nervous system damage, though evidence for this is disputed. The yaws treponeme comes next, causing skin and bone lesions. Finally, the pinta treponeme (*T. carateum*) causes only lesions of the skin. The treponemes of bejel, yaws, and pinta are not transmitted congenitally. Listed in this order, the treponemes can be looked upon as demonstrating a spectrum of natural attenuation, and there is epidemiological evidence to suggest that infection with one provides immunity to infection with another. Thus Rae (1951) reported that in Tonga, Fiji, and Samoa, where yaws was endemic, syphilis was rare. Hackett (1946) reported from Uganda that in Lira, 21 per cent. of the population had yaws whereas only 1 per cent. had venereal syphilis, while 200 miles away in Masaka 2 per cent. had yaws but 18 per cent. had venereal syphilis. Findlay (1946) reported that syphilis was of frequent occurrence and that yaws was rare in Northern Nigeria, but in Southern Nigeria yaws was common and syphilis was rare. Hewer (1946) reported that yaws was common in Southern Sudan and venereal syphilis in Northern Sudan.

There is experimental evidence to support the suggestion of cross-immunity (Table II). Medina (1963) reported that nineteen patients with untreated pinta were challenged with yaws treponemes; no infection and no increase in the reagin titre resulted; 233 healthy controls were also inoculated with yaws treponemes and all of them became infected, all undergoing uniform histological and serological changes.

TABLE II  
EVIDENCE OF CROSS-INFECTION

Untreated Original Disease	Challenging Treponeme	Number of Patients Challenged	Number of Patients becoming Infected by Challenging Treponeme
Pinta (various stages)	Yaws	19	0
Yaws (late)	Yaws	65	0
Yaws (early)	Yaws	18	1
Syphilis (various stages)	Yaws	133	8
Syphilis (various stages)	Yaws	10	0
Syphilis (late)	Yaws	40	1
Syphilis (late)	Bejel	8	0
Bejel (early)	Bejel	2	0
Syphilis (latent)	Syphilis	5	0

Turner (1936), while in Jamaica, reported that eighteen patients aged 2 to 11 years with untreated yaws were inoculated with treponemes from their

own lesions; only one developed a new lesion at the inoculation site. Medina (1963), in the study previously mentioned, described how 65 patients with late yaws were challenged with heterologous yaws treponemes; all failed to become infected and there was no increase in reagin titre. Medina also found that, out of 133 patients with untreated syphilis in various stages who had been challenged with yaws treponemes, only eight became infected; all of these were at the stage of early syphilis.

Turner (1936) also reported that no infections resulted when ten syphilitic patients were inoculated with yaws treponemes. Schaar (1933) reported that when forty neuro-syphilitics were inoculated with yaws treponemes only one became infected. Akrawi (1949) reported that eight patients with late syphilis were challenged with bejel treponemes and no infections resulted. As controls he used ten volunteers with no history of syphilis and repeated negative results to serum tests; when they were inoculated with bejel treponemes eight of them became sero-positive, producing erosive lesions at the site of the inoculation. In the same study Akrawi attempted to superinfect two bejel patients with bejel treponemes, and both attempts failed. As previously stated, Magnuson and others (1956) reported that five patients with latent syphilis were challenged with syphilis treponemes but no re-infections resulted.

From these studies it is clear that infection with one of the above-mentioned treponemes does provide a degree of immunity to infection with some or all of the other treponemes. The least pathogenic of the treponemes is *Treponema carateum*, which causes only lesions of the skin. It is suggested that with the pinta treponeme, much of the work of attenuating *Treponema pallidum* as a step in the elaboration of a vaccine, has already been done.

### Summary

A major step in evolving a vaccine against syphilis is the production or discovery of an attenuated treponeme capable of producing an effective immune response with the minimum of disease. There is clinical evidence to show that the treponemes of syphilis, bejel, yaws, and pinta present a spectrum of natural attenuation, and there is epidemiological and experimental evidence that protection against one disease is afforded by infection with the others. It is suggested that much of the work needed to attenuate *Treponema pallidum* has already been performed naturally during the

evolution of *Treponema carateum*. Further studies on this organism are justified and may well be fruitful.

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**La recherche d'un vaccin contre la syphilis**  
**Une approche épidémiologique**

## RÉSUMÉ

Un pas important à l'élaboration d'un vaccin contre la syphilis est la production ou la découverte d'un tréponème atténué capable de produire une réponse immunisante efficace avec un minimum de maladie. Il existe des preuves cliniques pour démontrer que les tréponèmes de la syphilis, du bejel, du pian et du pinta présentent un spectrum d'atténuation naturelle, et aussi des preuves épidémiologiques et expérimentales que la protection contre une de ces maladies est offerte par une infection causée par les autres. Il est suggéré que la plupart du travail nécessaire pour atténuer le *Treponema pallidum* ont déjà été faits naturellement pendant l'évolution du *Treponema carateum*. D'autres études concernant cet organisme sont justifiées et pourraient bien être fructueuses.